REMARKS/ARGUMENTS

Summary of Current Claim Amendments

Claims 1-5, 7, 8 and 22-29 are pending. Claims 1, 22 and 26 are currently amended.

Independent claims 1 and 22 have been amended to specify that the filtering occurs by passing the sample from a first chamber through a filter to a second chamber, forming a filtered sample containing particles that are the size of the analyte or smaller than the analyte in the second chamber while particles larger than the analyte are retained in the first chamber. These claims now also specify that a reagent that is able to specifically form a reagent-analyte particle complex is added to the second chamber, the filtered sample is then filtered to remove particles smaller than the reagent-analyte particle complex, thus forming a further filtered sample. The further filtered sample is then tested for the presence of any residual particles, the residual particles indicating that the reagent-analyte particle complex was formed, the presence of which is a positive indicator that the analyte (human immunodeficiency virus) is present in the sample fluid. These amendments are consistent with the language of previously presented independent claim 26.

Independent claim 26 has been amended to specify that the reagent specifically interacts with the analyte and to specify that the absence of a residue of the reagent-analyte particle complex is indicative of the absence of the analyte (human immunodeficiency virus) in the sample fluid.

Support for these amendments is found at least at paragraphs [0024] to [0037] and Figures 1 to 4 of the application as originally filed.

Interview Summary

Applicant thanks Examiner Skowronek for the courtesy of a telephone interview with its representatives, Matthew Zischka and Sally Hemming, and with inventor David

Farrow on January, 2008. References Tullis et al. (American Clinical Laboratory, pp. 22-23, 2001) and Chou et al. (US 20040072278) were discussed, although no consensus was reached during the telephone conference.

Withdrawal of Previous Rejections

Applicant thanks the Examiner for withdrawal of the rejection under 35 USC 112, the rejection under 35 USC 102 based on Ambrus and the rejections under 35 USC 103 based on King et al. in view of Coller et al.; King et al. in view of Coller et al. and in further view of Peterson; and Hanna et al. in view of Bernhardt et al.

Present Claims

Claim 1 of the instant application claims a method for detecting the presence of an analyte particle in a fluid.

The method comprises sequentially:

(1) filtering a sample of said fluid from a first chamber to a second chamber through a filter sized to pass said analyte particle and particles smaller than said analyte particle, retaining in said first chamber particles in said sample larger than said analyte particle thereby forming in said second chamber a filtered sample;
(2) adding to said filtered sample in said second chamber a reagent that specifically interacts with said analyte particle to form a reagent-analyte particle complex that is larger than said analyte particle;
(3) filtering said filtered sample from said second chamber through a filter sized to pass particles that are smaller than said reagent-analyte particle complex thereby forming in said second chamber a further filtered sample; and
(4) testing said further filtered sample in said second chamber for the presence of residual particles, wherein the presence of said residual particles identifies the presence of said reagent-analyte particle complex in said second chamber, and wherein the presence of said-analyte particle complex is indicative of the presence of said analyte particle in said fluid and wherein the absence of said

reagent-analyte particle complex in said second chamber is indicative of the absence of said analyte particle in said fluid.

As stated in the response to the previous Office Action, the claimed method relies on two size exclusion filtering steps, with an intermediate step of affinity complexing the analyte particle in order to increase the apparent size of the analyte particle, thus changing the fraction in which the analyte particle is found from one filtering step to another. The presence of residual reagent-analyte particle complex in the sample is used as an indicator that the analyte particle is present in the original fluid. Thus, the present methods test directly for the presence/absence of the reagent-analyte particle complex, the result of which direct test is used to indirectly indicate the presence/absence of the analyte particle in the original fluid.

Claims 22 and 26 include the features of claim 1, but are narrower in scope than claim 1. For example, claims 22 and 26 specify that the analyte particle is human immunodeficiency virus. Thus, claims 22 and 26 also incorporate a two-step size exclusion filtering process with an intermediate affinity complexation step, with a final direct test for the presence of residual particles that signify the formation of the reagent-analyte particle complex, which is used as a proxy to indicate the presence of the analyte particle itself. The final direct test occurs within the chamber in which the reagent-analyte particle complex is formed.

The present methods have the advantage of providing an easy, efficient and rapid method that allows for detection of an analyte particle in a small sample volume, within a single device without the need for external testing beyond that which occurs within the device itself. The present methods eliminate the need to collect a final filtrate sample in order to detect the presence of an analyte particle, or the need to extract an analyte particle that may be captured by treatment with an immobilized reagent molecule. By combining the formation of a reagent-analyte particle complex with a second size exclusion step that retains such a formed complex, a single step is performed that accomplishes the dual goals of separation of smaller particles and the step of collection for the purpose of detection. Applicant submits that these advantages are not described by, nor are obvious in light of, any of the references identified by the

Examiner, alone or in combination, including for the reasons set out in the arguments below.

Claim Rejections—35 USC 102

The Examiner has rejected claims 1 to 5, 22 and 26 under 35 U.S.C. 102(b) as being anticipated by Tullis et al. In particular, the Examiner asserts that Tullis discloses a method of filtering HIV particles (equated to analyte) from blood using a filter that separates the cells (particles larger than HIV) from the HIV, allowing further passage of particles that are smaller than the viral-reagent complex and testing for the presence of the viral-reagent complex. In particular, the Examiner asserts that the use of PCR methods to detect reagent-analyte particle complex does result in the detection of the presence of virus-reagent complex.

The Applicant respectfully disagrees that Tullis anticipates the present claims, for at least the following reasons.

First, Tullis describes the same device as described in Ambrus. Given that the Examiner has withdrawn the rejection based on Ambrus, Applicant points out that use of the Tullis device alone cannot anticipate the present claims.

Thus, Applicant assumes that the Examiner's rejection is based on the comment in Tullis that the effectiveness of the device was subsequently tested by extracting RNA from virus trapped on the column and conducting PCR analysis.

Applicant submits that this does not constitute testing a further filtered (i.e. twice filtered) sample for the presence of a reagent-analyte particle complex, the testing performed within the chamber in which the reagent-analyte particle complex is formed. Extraction of RNA from trapped virus would destroy any complex formed between the antibody (reagent) in the cartridge. As well, the PCR analysis can only detect the presence of the virus itself, since the antibody will not contain any RNA and cannot be detected by nucleic acid polymerase chain reaction amplification methods. Furthermore, neither of these detection methods is performed within the chamber in which the reagent-analyte particle complex is formed. Thus, at most Tullis describes

removal of the virus (analyte) away from any reagent-virus complex that has been formed, with subsequent detection of the virus alone.

In contrast, the present claims now clarify that the physical presence of the reagent-analyte particle complex is directly detected within a chamber of the device and used as an indirect indicator of the presence of the analyte particle in the original fluid. Since Tullis does not include this element, Tullis therefore cannot anticipate the present claims.

Furthermore, Applicant submits that subsequent testing for an isolated analyte molecule by PCR, removed from the filtering steps of the present claims and removed from the formed reagent-analyte molecule formed within the device used to filter the sample, is no different than testing for the analyte directly in a sample using RNA extraction and PCR methods without first conducting the filtering and affinity complexing of the present method. In doing so, the advantages provided by the presently claimed methods, including the ease, efficiency, speed and ability to test a small sample volume, are lost, and a sample may as well be subjected to known analysis methods involving RNA extraction and subsequent PCR analysis in order to detect the presence of a virus analyte particle.

Thus, although the Examiner argues that detection of the analyte alone is the same as detection of the reagent-analyte particle complex, Applicant submits that isolating the analyte molecule away from the device, directly detecting the analyte particle and using its detection as an indicator of the formation of a reagent-analyte particle complex, as is described in Tullis, is the opposite of, and serves to negate the purpose of, the detection employed in the presently claimed methods.

For all of the above reasons, Applicant submits that Tullis simply cannot anticipate current claims 1, 22 and 26. Since claims 2 to 5 depend directly or indirectly from claim 1, Applicant submits that these claims are also not anticipated by Tullis.

Applicant therefore respectfully requests withdrawal of the rejection under 35 USC 102(b) based on Tullis.

Claim Rejections – 35 USC 103

(i) 103 rejection base on Tullis in view of Bernhardt and in view of Peterson

The Examiner rejected claims 1 to 5, 7, 8 and 22-29 as obvious over Tullis et al. in view of Bernhardt et al. and in view of Peterson et al. In addition to the comments provided in the rejection based on Tullis under 35 USC 102, the Examiner states that Bernhardt describes formation of virus-ligand complex using CD4 receptor (reagent) to bind HIV (analyte particle) and that Peterson shows an injection molded plastic filtration device. Particularly, the Examiner indicates that it would have been obvious to modify the device of Tullis with the CD4 reagent of Bernhardt and the molded plastic of Peterson.

Applicant respectfully disagrees, for at least the following reasons.

For the reasons given above, Applicant submits that Tullis does not disclose or suggest detection of the physical presence of a reagent-analyte particle complex within a chamber in which the reagent-analyte particle complex is formed, as is required in independent claims 1, 22 and 26 of the present application. At most, Tullis describes isolation or removal of an analyte particle away from any reagent molecule, and then subsequent testing to confirm the presence of the analyte particle (not a reagent-analyte particle complex).

Bernhardt also does not disclose detection of a reagent-analyte particle complex within the chamber in which the reagent-analyte particle complex is formed. Bernhardt is concerned with removing viral particles from a sample to clean the sample, and is not concerned with testing to confirm whether any analyte particle has been complexed with a reagent molecule. Rather, Bernhardt relates to a method for removing viral particles from an aqueous protein solution, and is mostly concerned with providing a resultant decontaminated protein solution free from virus. Examples 1 and 2 of Bernhardt (columns 3 and 4) describe testing the filtrate after filtration, which would contain particles smaller than any reagent-analyte particle complex, but would not contain any reagent-analyte particle complex itself. Thus, the approach described in

Bernhardt requires the additional steps of collecting filtrate and then detecting the analyte in the filtrate once collected.

Even if Peterson does disclose injection molded plastic filter device, such a disclosure is not sufficient to overcome the deficiencies of Tullis in combination with Bernhardt, namely the lack of disclosure of testing for the presence of a reagent-analyte particle complex within the chamber in which such a complex is formed in order to identify the presence of an analyte particle in the original fluid. Thus, Peterson cannot combine with Tullis and Bernhardt to render the subject matter of the present claims obvious.

Applicant therefore requests withdrawal of the rejection under 35 USC 103 based on Tullis et al. in view of Bernhardt et al. and in view of Peterson et al.

(ii) 103 rejection base on Chou in view of Bernhardt

The Examiner rejected claims 1 to 5, 7, 8 and 22-29 as obvious over Chou et al. (US 2004/0072278) in view of Bernhardt et al. The Examiner states that Chou shows a microfluidics particle analysis system having size selective channels, which the Examiner asserts reads on filtering out particles larger than the virus and smaller than the virus.

Applicant respectfully disagrees that the combination of Chou et al. and Bernhardt et al. render the subject matter of the present claims obvious, for at least the following reasons.

As stated above, in contrast to the present claims, Bernhardt does not describe or suggest detecting the physical presence of a formed reagent-analyte particle complex within the chamber in which the reagent-analyte particle complex is formed, the presence of which is then used to identify the presence of the analyte particle in the original fluid sample.

The Chou reference does not compensate for this defect in Bernhardt. Although the Examiner indicates that Chou describes filtering out particles smaller than the virus (analyte particle), this is irrelevant to the presently claimed methods. Chou does indicate that larger particles can be separated from smaller particles, and does indicate that once a particle has been retained in the described microfluidics device, such a particle can be analyzed by various methods, including exposing the particles to desired reagents. However, the present claims make use of a reagent molecule to assist in the retention and separation of a desired analyte particle through the formation of a reagent-analyte particle complex, and then detect the physical presence of a formed reagent-analyte particle complex within the chamber in which the complex is formed to act as an indirect indicator of the presence of the analyte particle in the original fluid. Chou does not describe or suggest contacting an analyte particle with a reagent molecule to form a complex prior to further size filtration steps, nor detection of the formed complex within the chamber in which the complex is formed.

Thus, Applicant submits that Chou cannot combine with Bernhardt to render the present claims obvious, since neither reference nor the combination of the two references describes or suggests the approach of using a reagent molecule to assist in two-step size exclusion filtration in combination with direct detection of a reagent-analyte particle complex within the chamber in which the complex is formed to indirectly identify the presence of the analyte particle.

For these reasons, Applicant respectfully requests withdrawal of the rejection under 35 USC 103 based on the combination of Bernhardt et al. in view of Chou et al.

Summary

In fact, none of the references identified by the Examiner describe or suggest indirect identification of an analyte particle by direct detection of the physical presence of a reagent-analyte particle complex, particularly detection within a chamber in which such a complex is formed, as specifically required by present claims 1, 22 and 26. Applicant submits that the entire combined approach as presently claimed would not have been obvious to a skilled person, given that the references identified by the Examiner all either describe direct detection of the analyte particle itself, either in the

effluent/filtrate following filtration or by extraction from an immobilized complex, or do not even suggest that detection of an analyte particle is relevant. A skilled person would not have been led to combine size exclusion filtration with formation of a reagent-analyte particle complex, followed by a second size filtration step and detection of the formed complex within the chamber in which the complex is formed as an indicator of the presence of the analyte particle, thus eliminating the need to further collect effluent/filtrate or extract a captured analyte particle in order to directly detect the analyte particle itself.

In view of the foregoing, it is believed that this application is in condition for allowance. Favourable reconsideration and allowance of this application are requested.

Respectfully submitted,

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S&B File ref. 93292-1